IX. Program Planning and Evaluation Issues

Costs and Benefits of Short-Course Perinatal AZT Intervention

Presented by Elliot Marseille, Dr.P.H., M.P.P.
University of California, San Francisco

The purpose of this presentation is to provide an assessment of the economics of preventing vertical transmission in low- and in middle-income countries. My aim is to frame this information in a way that supports sound resource allocation decisions among various program options. To achieve this, we focus on three research questions:

1. Can antiretroviral therapy to reduce vertical transmission be cost effective? Another way of stating this question is: Does the allocation of funds to an antiretroviral program produce the same or greater health benefits than an allocation of those same funds to alternative prevention programs?
2. How does a replacement-feeding program affect combined HIV-related and non-HIV-related mortality in the infants of HIV-infected mothers? As you know, there are competing mortality risks for HIV-infected infants. In a breast-feeding population, you have the risk of HIV transmission, and in a replacement-feeding regimen you have competing mortality risks from non-HIV-related causes.
3. If replacement feeding decreases total net deaths from these two sources, what are the cost and cost effectiveness of such a program in combination with a prenatal antiretroviral program?

I would like to look first at the antiretroviral cost-effectiveness analysis. The intervention that we modeled is the Thai/CDC AZT regimen that we have heard so much about in recent months and at this workshop. We examined the cost effectiveness of this program in two settings: a high HIV-prevalence setting, such as might be found in rural Tanzania, and a low HIV-prevalence setting, such as that found in urban Thailand. Note also that the Tanzania setting represents a low-income environment, and urban Thailand a relatively affluent setting.

We evaluated costs from the perspective of a public-sector health care payer, such as a ministry of health in these two countries. We assessed the costs of the counseling and testing, and of the drugs themselves.

Outcomes are evaluated using two standard outcome measures: the cost per case averted and the cost per DALY. I know that there are some people who are very familiar with the basic concepts of economic appraisal of prevention programs, and there may be people who are less familiar. So I want to briefly digress and explain some of the concepts concerning this evaluation, which may be useful in understanding what follows. I would like to begin by looking at the concept of a DALY and relate that to the question of how one

would determine whether an antiretroviral program is cost effective.

A DALY is a measure of program benefit, and it stands for Disability-Adjusted Life-Year. It is equivalent to the number of years of life generated by an intervention. Those life-years are then weighted by two factors: The first is the quality of life enjoyed by the beneficiary of the program. The second weight reflects the economic value of that year of life.

Regarding the quality-of-life weight, a year of life in somebody who is quadriplegic would be valued at a lower rate than a year of life enjoyed by somebody in perfect health. The economic value of a year of life generated by a program depends upon the productivity of that person. For example, a life-year for a 25-year-old woman who is the social and economic backbone of her family would be valued at a higher rate than a life-year of an 80-year-old person who no longer can care for other members of the family.

Why use DALYs? There are two principal advantages of using this measure of program benefit. The first is that it takes duration of benefit into account. The second is it puts different interventions on the same metric, so that it becomes possible to compare the benefits of an HIV prevention program with other HIV and non-HIV options. Using the metric of DALY, you could compare the benefits of an HIV program with a diarrheal disease control program or an immunization program.

In this table we compiled the cost effectiveness of a range of well-accepted public health programs, both HIV prevention programs and non-HIV prevention programs. I want to draw your attention to a few of them. Among the HIV prevention options, an extremely cost-effective program is the improved detection and treatment of STDs in adults. These data come from the Mwanza study in Tanzania where the cost per DALY was calculated at $13.

Blood supply screening for HIV using a rapid lab test costs between $1 per DALY and $250 per DALY. For the two countries we have focused on here, Tanzania and Thailand, the cost effectiveness of this program is $60 and $200, respectively.

Information, education, and communication programs to promote behavior change and condom use also range widely from $1 per DALY to $150 per DALY. This variation is due to differences in HIV prevalence, sexual behavior, and STD co-factors.

Looking at non-HIV programs, immunization for polio plus DPT costs about $20 per DALY in a high mortality area and $40 per DALY in a low mortality area. River blindness control in Burkina Faso costs somewhere between $200 and $300 per DALY, depending on the breeding pattern of the vector and other factors.

So what can one derive from this chart? I think there are two messages that it suggests. The first is that there is a wide range of cost-effectiveness estimates for well-accepted public health interventions. So it really is not possible to draw a firm cut-off line above which you say a program is necessarily cost effective and below which you say it is not.

The second message is that it still is possible to draw some conclusions about the

range of cost effectiveness that one would like to see in a program that one commits funds to. Less than $100 per DALY is very likely to be an attractive option in either of these two settings, that is, Thailand or Tanzania. A program that falls in the range of $100 to $200 per DALY is probably okay, particularly in Thailand, but possibly in a low-income setting such as Tanzania as well. Much above $200 per DALY begins to become questionable as to whether investment in such a program would produce health benefits that are competitive with other possible uses of those funds.

I would like to return to the antiretroviral analysis and pick up the thread by looking at the value of some of the key inputs that determine the cost effectiveness of the antiretroviral intervention according to our model. For the estimate of antiretroviral efficacy, we use the 50 percent relative reduction found in the Thai trial. This represents a reduction in Tanzania from a background transmission rate of 22 percent down to 11 percent, and in Thailand a reduction from 18.6 percent to 9.3 percent transmission. Prevalence of HIV among pregnant women was taken at 15 percent in Tanzania and 2.4 percent in Thailand, which is the approximate national HIV prevalence. We also looked at the effect of this program in a high-prevalence area of Thailand, such as is found in the northern parts of the country where prevalence is approximately 5 percent.

The cost of voluntary counseling and testing is a surprisingly hard figure to nail down. Based on data from a voluntary counseling and testing program in Zambia, we used $4 per woman in Tanzania and extrapolated from this figure an estimate of $12 in Thailand. Completion rates for voluntary counseling and testing were assigned a value of 60 percent: Of women who begin a pre-test counseling session, 60 percent are assumed to complete the testing and return for their results and post-test counseling. Of the 60 percent who complete counseling and testing, we posit that 75 percent would then accept to begin an antiretroviral treatment. These figures are based on the experience of the PETRA trials now underway in Africa.

The cost of AZT was set at the rate recently announced by Glaxo Wellcome of about 25 percent of industrial world prices, or roughly 75 cents per dose. The lifetime cost of treating children who otherwise would have gotten HIV/AIDS is about $195 in Tanzania and $1,300 in Thailand. Life expectancy for non-HIV-infected women is 52½ years in Tanzania and about 70 years in Thailand. Health benefits were discounted at a rate of 5 percent per year.

We assume no breast-feeding in this model, because later we will look at the economics of a combined antiretroviral and breast-feeding regimen.

The results indicate that in Tanzania such a program would cost about $30 per DALY. This is likely to be extremely attractive. In Thailand, we looked at the results under three different scenarios. The base-case scenario assumes the national HIV prevalence rate of about 2.4 percent, and under that circumstance the cost per DALY is roughly $360. This is probably not going to be a very cost-effective regimen at this HIV-prevalence rate.

However, if the intervention is targeted to higher prevalence areas, such as in the

Phayao area where prevalence is about 5.2 percent, the situation changes dramatically. The cost per DALY drops to $145, and this then is likely to becomes an attractive option.

Finally, we looked at a somewhat speculative no-voluntary-counseling-and-testing option. In areas where a large number of women have known HIV-positive status from previous testing, it might be possible to carry out the program with very limited additional testing and counseling. If feasible, such an approach would yield a savings of roughly $39 per DALY. These savings come from the averted medical costs of children who otherwise would have become HIV infected.

Now let us look at the cost effectiveness of a replacement-feeding regimen. The model that we constructed assesses the month-by-month risk of fatal events for alternative infant feeding strategies. We considered five feeding strategies:

- The current feeding regimen in these two settings
- Breast-feeding only for 24 months
- Breast-feeding for 6 months, followed by weaning
- Breast-feeding for 3 months, followed by normal weaning
- Replacement feeding for the full 24 months

We start with the assumption that of 100 infants born to HIV-infected mothers, a certain proportion are infected during pregnancy and delivery. We estimate this proportion for two situations: (1) in the presence of an antiretroviral program and (2) where there is no antiretroviral program present. The remainder of the infants are at risk for the two types of fatal adverse events that we have discussed, that is, non-HIV-related death and HIV transmission. We then estimate the risk of adverse events for each month of life, keeping track of survival by age in months for the non-HIV-infected child. A child who is HIV-infected and dies later of non-HIV-related causes is counted as only one adverse event.

On this overhead we see the value for some of the key parameters that affect the cost of the replacement feeding intervention. We posit a 60 percent program acceptance rate. We looked at costs under two scenarios: one, a standard replacement feeding program, and the second, a comprehensive replacement feeding program that has enhanced program inputs and ancillary supports.

There is a lot of debate and uncertainty about what it is going to take to do a replacement-feeding program correctly so as to minimize spillover effects into the HIV-uninfected population. We therefore considered these two versions: a less expensive standard model and a more expensive approach–what we are calling a comprehensive model.

There is a significant difference in the intensity of inputs in these two approaches. For example, the number of training sessions needed to train counselors in replacement-feeding counseling is assumed to be five in the comprehensive model and four in the standard model. In the comprehensive model, we assume 12 follow-up visits to mothers who have accepted the program and, in the standard model, only 6 such follow-up visits.

The cost of formula-feeding for the first 6 months is $78 under both regimens. This price is based on the wholesale price of formula food in Johannesburg. From 7 months to

24 months in the comprehensive program, we are looking at $20 in cow milk replacement, and in the standard model it is assumed that the family would assume that cost.

Because we anticipate there may be increased morbidity in the replacement feeding children, we modeled the expected cost of the anticipated increased medical care utilization. We assumed five additional outpatient visits for the replacement-feeding children in Tanzania and about one in Thailand, and 0.2 hospital admissions in Tanzania and only 0.004 hospital admissions in Thailand.

The program would also provide $10 in contraception during the 6 months that the mother would otherwise have benefit of naturally if she were breast-feeding.

We then estimated the HIV-transmission risk during breast-feeding by looking at published and unpublished data. These estimates of transmission are based on studies comparing breast-feeders or non-breast-feeders in Africa, with a conservative extrapolation to Thailand. With antiretroviral use, the transmission is increased slightly to reflect the greater percentage of newborns at risk. Temporal patterns of risk are portrayed using a mathematical risk function so that late postnatal risk is consistent with a meta-analysis conducted by the Ghent group on mother-to-child transmission.

These figures of the 0- to 24-month transmission risk and the late postnatal transmission risk are consistent with the figures from the Grace Jones analysis.

Turning now to non-HIV-related mortality, these mortality rates are estimated from studies conducted in Thailand and Tanzania. Based on estimates from a well-controlled Malaysian study, the relative risk of formula-feeding versus breast-feeding is taken at 4.0 for Tanzania. For Thailand we assumed a lower figure, 3.0, since this is a relatively affluent area.

Given these mortality estimates, the 24-month survival curves under each of the five feeding strategies that we modeled are shown in the following two charts.

This chart shows the survival curves for rural Tanzania for each of the five feeding strategies. The most important thing to note in this chart is that for the whole 24-month period, exclusive replacement feeding yields the lowest rate of fatal events of all of the strategies. Current breast-feeding patterns in Tanzania, represented by the lowest line, produce the most fatal events.

We see a similar pattern in Thailand where the highest mortality rate would result from breast-feeding for the full 24 months, and the lowest mortality rate for the full 24 months would result from exclusive replacement feeding.

In numerical terms, the number of fatal events associated with current feeding patterns in Tanzania is about 32, and 10 in Thailand. With universal replacement feeding, those figures dropped to 23.5 and 2.7 events in Tanzania and Thailand respectively, so that you have a savings of 8.7 and 7.5 fatal events in each of these two settings.

Looking now at a summary cost-effectiveness figure for the formula-feeding program alone, in the comprehensive program in Tanzania, we estimate that the cost-effectiveness ratio would be $97 per DALY and in Thailand, a lower figure, about $57 per DALY.

If the standard programs were found to be adequate, the cost effectiveness increases somewhat, to $70 per DALY in Tanzania and a very low $14 per DALY in Thailand. Much of that low figure again can be attributed to the savings in medical care costs for infants who otherwise would have contracted HIV.

Combining the cost effectiveness of the antiretroviral treatment and the replacement-feeding formula yields an overall cost effectiveness of the combined intervention of $64 in Tanzania, assuming the comprehensive program, and $284 in Thailand under the comprehensive program.

Using the standard program, you get higher levels of cost effectiveness, that is, $53 per DALY in Tanzania, and $132 per DALY in Thailand.

I think we can draw three conclusions from this modeling exercise: One is that antiretroviral therapy can be a cost-effective intervention in Tanzania. In Thailand, cost effectiveness depends on targeting the intervention to areas of relatively high HIV prevalence and/or achieving low costs for counseling and testing. Second, for the postnatal period, replacement feeding averts deaths for infants of HIV-infected mothers in both Tanzania and Thailand. Third, replacement feeding can be cost effective when paired with prepartum antiretroviral treatment in both countries.

Assessment of HIV Prevalence in Antenatal Populations in a Developing Country Setting

Presented by Kassim Sidibe, M.D.
Projet RETRO-CI

In the first presentation of this workshop, Dr. Dondero provided a lot of data on HIV prevalence in antenatal clinics throughout the world. What we do not know about this data is where they were collected in each individual country and how they were collected. I am not saying that I have a problem with this data; I am just asking some questions.

I am going to describe to you the experience we have had in Ivory Coast in the assessment of HIV prevalence in antenatal populations. I would like to thank my colleagues from Projet RETRO-CI and the National AIDS Programme in Abidjan, Côte d'Ivoire, who were heavily involved in the work I will present.

Background (I)

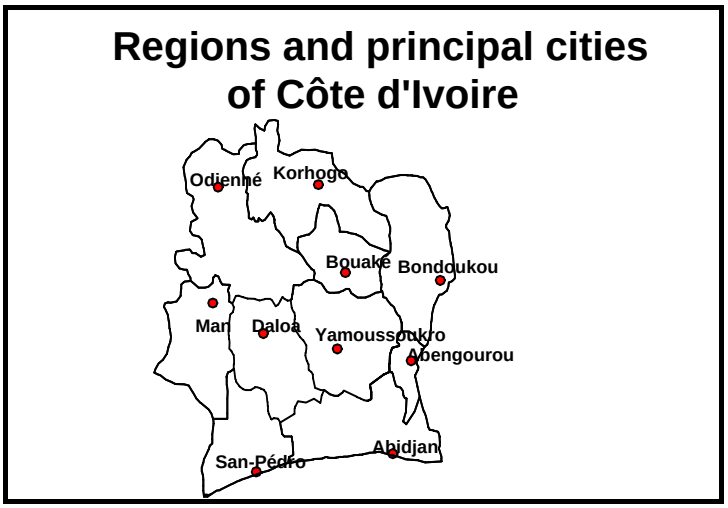
- Côte d'Ivoire: West African country with a population of 15 million
- Ministry of Public Health includes 10 administrative regions
- National AIDS control program coordinates AIDS prevention and surveillance activities
- Ministry of health antenatal clinics exist in all the regions of the country (at least one/city)

Côte d'Ivoire is a West African country with a population of about 15 million. The Ministry of Public Health includes 10 administrative regions for the National AIDS Programme, which coordinates AIDS prevention and surveillance activities. In all the administrative regions, there is at least one antenatal clinic in each city.

Background (II)

- Côte d'Ivoire is heavily affected by the HIV/AIDS epidemic
- More than 37,500 AIDS cases reported
- Lack of nationwide HIV prevalence data
- In 1997, initiation of national sentinel HIV serosurveillance program

Côte d'Ivoire is heavily affected by the HIV epidemic. More than 37,000 AIDS cases have been reported since 1987. HIV prevalence data exist for many years for Abidjan, the capital city, but there are no nationwide HIV prevalence data. In 1997 the National AIDS Programme initiated a national sentinel HIV serosurveillance program.

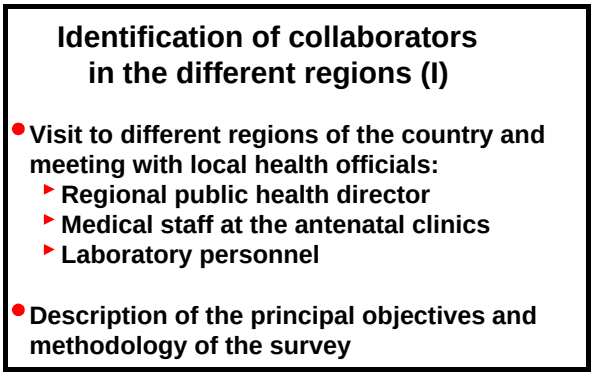


This map shows different regions of Côte d'Ivoire and the capital city. The two most important cities, Abidjan in the south and Bouake in the center, each have more than one public antenatal clinic. In each of the other cities, there is only one antenatal clinic.

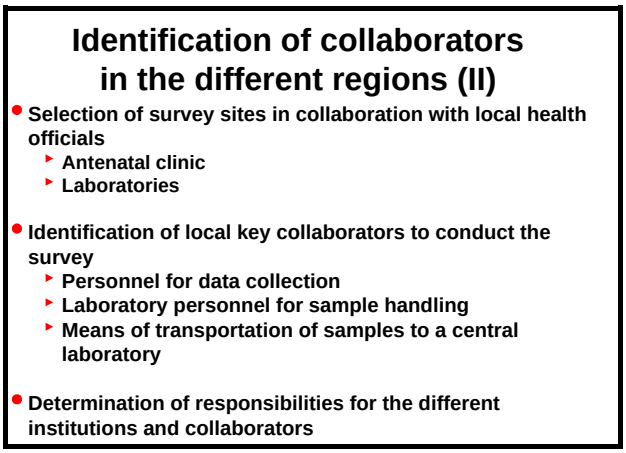
Steps in the implementation of HIV prevalence assessment

- **Identification of a central laboratory for HIV testing**
- **Visit of potential serosurveillance sites in all the 10 regions**
- **Selection of survey sites**
- **identification of local collaborators**

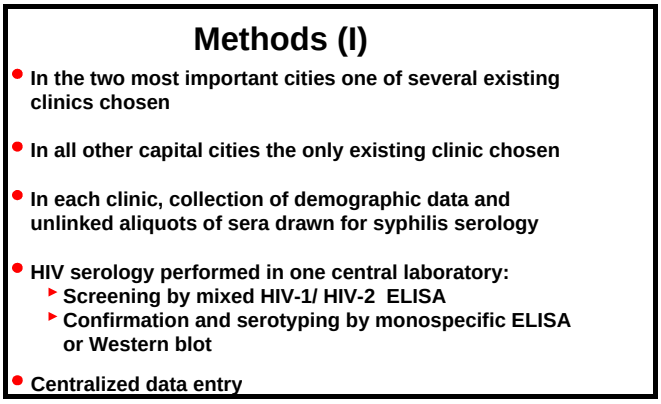
Before going into detail, I will outline the different steps we took in conducting this HIV prevalence assessment. First, the National AIDS Control Programme selected a central laboratory for HIV testing. We chose a Projet RETRO-CI laboratory for quality consistency purposes. Second, we visited all the potential surveillance sites in all the 10 regions to make an assessment of the health care facilities. Third, we selected one antenatal clinic and a laboratory in each of the 10 regions. The laboratory was selected in each city to perform a syphilis test. Finally, we identified local collaborators to coordinate the survey and to do the field work in each city.



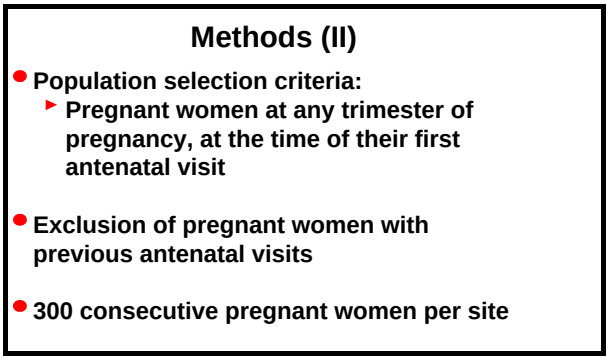
In each region, we organized a meeting with the regional public health director, the medical staff of the antenatal clinic selected, and the laboratory personnel. We explained to them the principal objectives and methodology of the survey. In Côte d'Ivoire, syphilis serology is done routinely during pregnancy. The test costs about $2. We offered to do this serology test free of charge for approximately 300 pregnant women per clinic, with the National AIDS Programme providing all the equipment needed for the syphilis tests.



We selected 10 antenatal clinics as well as the laboratories in collaboration with the local health officials. In each clinic and laboratory we identified local key collaborators for data collection and syphilis serology. We also identified means for transportation to the central laboratory and determined responsibilities for each physician and for health personnel.



This figure outlines the method we used. In the two most important cities, only one of several existing clinics was chosen. In all other cities, the only existing clinic was chosen. On each patient, we collected demographic data: age, country of birth, marital status, schooling, and gestational age. We also collected an aliquot of serum drawn for syphilis serology and permanently removed personal identifying information from it. These samples were sent to the central laboratory for HIV testing. Screening was done by mixed ELISA; confirmation and viral typing was done by monospecific ELISA or Western blots. Data entry was also centralized.



This figure shows the selection criteria for the surveillance blood specimens. We included pregnant women at any trimester of pregnancy at the time of their first antenatal visit. We excluded pregnant women with previous antenatal visits. We collected data and blood specimens consecutively from about 300 pregnant women at each site.

Development of survey activities

- Survey carried out from May to October 1997
- Mean duration per site: 6 weeks (range 2-12 weeks)
- One person at each site responsible for field work
- Supervision: one week/site

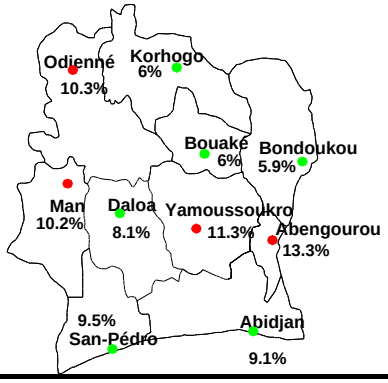
The first survey was carried out from May to October 1997. The mean duration per site was 6 weeks, with a range from 2 to 12 weeks. We had one person at each site responsible for field work. The study coordinator was responsible for supervision for 1 week at each site.

HIV prevalence among pregnant women by serotype (N=3045)

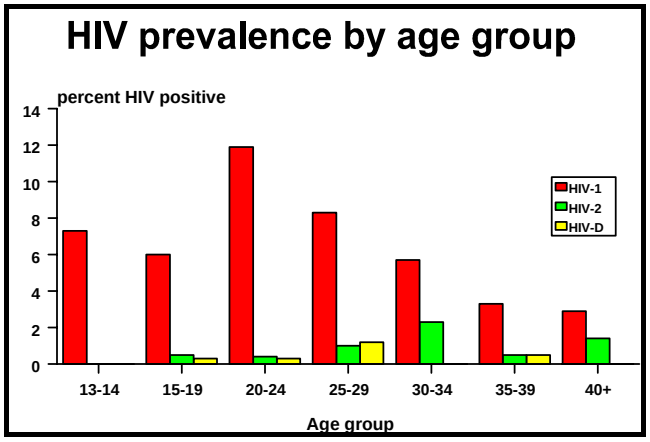
- 7.8% HIV-1 positive
- 0.8% HIV-2 positive
- 0.4% HIV-D positive

This figure summarizes some results of the study that we conducted. A total of 3,045 women were tested for HIV infection. Overall, 7.8 percent were HIV-1 positive, 0.8 percent were HIV-2 positive, and 0.4 were HIV-D positive.

Geographic distribution of HIV prevalence in pregnant women in Côte d'Ivoire, 1997



This figure shows the geographic distribution of HIV prevalence among pregnant women in Côte d'Ivoire. Dots represent HIV prevalence of more than 10 percent. Squares indicate an HIV prevalence of less than 10 percent. HIV prevalence varied from 5.6 percent to 13.3 percent.



This chart shows HIV prevalence by age group. HIV-1 is in black, HIV-2 in gray, and HIV-D in light gray. HIV-1 prevalence is high in all the age groups, with a maximum of 12 percent in the age group of 20-24 years. HIV-2 is relatively low; it is rare before 25 years, and reaches a maximum in the age group of 35-39 years.

In conclusion, HIV prevalence assessment is feasible in antenatal populations for Côte d'Ivoire, and the system can be based on existing health care facilities. Repeat serosurveys will monitor trends in HIV prevalence and evaluate the impact of prevention activities.

Evaluating Program "Coverage" and Compliance with AZT Dosage and Evaluating HIV Transmission Rates in Prevention Programs

Presented by R.J. Simonds, M.D.
Centers for Disease Control and Prevention

I am not an evaluator, but I would like to offer some common sense suggestions for ways that we can begin to think about evaluation as programs are getting started. This workshop has highlighted many areas where perinatal HIV prevention programs can go awry, and we need to think about how to quickly identify those areas so we can provide feedback and make the programs more effective along the way.

Evaluating perinatal HIV prevention programs in developing countries

- goals of monitoring
- items to monitor
- possible data sources
- handling of data

I have taken the approach of conceptualizing the issue in terms of a cascade of events that occur in these programs. I would like to (1) discuss what the goals of monitoring and evaluation should be, (2) provide suggestions for some of the items that might be useful to monitor, (3) discuss possible data sources, and (4) raise issues related to handling of the data.

Goals of perinatal HIV prevention program evaluation

- determine program coverage
- determine program effectiveness
- determine program costs
- monitor trends in coverage, effectiveness
- prompt focussed studies of program failures

Evaluation can serve multiple purposes. First of all, you could look at some of the process of the program. You could determine how well the program is covering the population, including how many people are served, what proportion of the target population is being served, and what is the quality of the service being provided.

Second, if you can link your program evaluation with outcome data, you can determine the effectiveness of the program, which we all would agree is the bottom line of this kind of evaluation.

Third, if you can collect cost data, you can then begin to use more reliable numbers for cost-effectiveness analyses that are based on actual program experience.

Fourth, it would be important to monitor trends in these factors. Are there trends in coverage? Are there trends in effectiveness? In particular, it is important to monitor trends that would reflect the impact of modifications of the program done to improve it. For

instance, if different procedures are put into place, you can look at what the impact of those are.

Finally, seeing areas where the program is breaking down can generate ideas for focused research studies to look into these problem areas.

Considerations for monitoring perinatal HIV prevention programs

- How acceptable is data collection?
  - availability of existing data sources
  - ability to modify existing data collection
  - resources needed to collect new data
- What data are needed for decision making?
- What level of data quality, accuracy, timeliness is needed?

In thinking about what kinds of data to collect, you need to think about several things. I have tried to outline a few of the issues that should be considered when coming up with a "menu" of data items to collect. First of all, it is important to consider the acceptability in your program of the data that you would want to collect. As with the interventions we have been discussing, if you want the evaluation to be sustainable, it must be acceptable. We need to develop data collection strategies that are acceptable to the people who will be conducting the evaluation. This can mean an important limitation in terms of what data can be collected.

The first approach would be to try to look at what existing data sources there are and try to maximally use those things that already are in place to help you. Data such as vital statistics or serosurveillance that are in place for other purposes can be used to help evaluate your program.

Second, you need to consider whether there are ways that you can make relatively minor modifications to existing data collection that might help you to evaluate your programs. For instance, log books in delivery rooms might be modified to collect some additional data that would let you know directly how much coverage you are getting with your program.

Third, when you are thinking about collecting new data, you need to seriously consider what sort of resources are needed to do that. Everyone is aware that each new data collection step, particularly if it involves wide coverage of data collection, costs resources.

The second big concept is trying to focus on determining what data items are most necessary in your setting to help make decisions needed for the program. In moving from a more intensive research approach into program evaluation, it can be a difficult adjustment to

cut back on the data items that you are collecting. Rather than thinking, "Gee, it would be interesting to know this," you should be thinking, "we really need to know this because if this piece of data is showing this trend we need to act on it." Focusing the data collection on that which is necessary for decision-making is a very important consideration.

Finally, you should at least consider what level of quality and timeliness you really need for decision-making as you plan what data you are going to be collecting and how it will be collected.

With the next few slides, I want to outline some examples of data that could be collected that might balance the need for data for program evaluation with the potential availability of that data.

I have divided this up into two categories: the program process, that is, the provision of program services, and the program outcomes.

What to measure in perinatal HIV prevention program evaluation

- program services
  - antenatal care
  - counseling and testing
  - ZDV use
  - formula use
- program outcomes
  - infant infection
  - other outcomes

As far as the program services, this corresponds with the "cascade" approach of the main components of the programs such as antenatal care, counseling and testing, the use of ZDV or other antiretrovirals, the use of formula, as well as any other interventions that might come along and be added to the program.

Regarding outcomes, one of the important outcomes, of course, is infant infection. But there are others that I will get into in an upcoming slide.

Monitoring antenatal care utilization

- number of deliveries in population
- number of women receiving antenatal care
- gestational age at start of antenatal care

First, the antenatal care utilization: It is important to have data on the number of deliveries in the population, which represents an important denominator that will be

necessary for a number of evaluation indicators. You also would want to know the number of women who have received antenatal care–either any antenatal care or some threshold of antenatal care, but something that would be measurable. Given the fact that the interventions, particularly the short-course AZT intervention, are being initiated sometime during the prenatal period, you would want to know what proportion of women are coming in for antenatal care in time to take advantage of that. So some assessment of the gestational age at which women are coming in would be important.

There are other considerations that are not listed on the slide, such as other antenatal care quality indicators. For instance, you might want to measure the coverage of tetanus immunization or syphilis screening so that you could compare the coverage of HIV prevention with that of tetanus prevention or syphilis prevention to try to tease apart where your problems may lie.

Monitoring antenatal HIV counseling and testing

- number of women counseled
- number of women tested
- number of women returning for results
- number of HIV+ pregnant women diagnosed

The second area is antenatal counseling and testing. Knowing the number of women that are being served by your counseling program would give you an indication of what sort of resources are needed or are being used in terms of counselors, time, etc. The number of women counseled also provides a denominator for the second item, which is the number of women tested, so you can get an idea of what proportion of the women being approached for testing are being tested.

An additional issue is that of women returning for results. We have heard a lot about that, and it will be an important factor to monitor.

The last item is assessing the proportion of HIV-infected childbearing women who were identified through the counseling and testing process. This requires comparing the number of positive tests in your counseling and testing program with estimates of the number of infected women delivering, such as could be obtained from serosurveillance data. This then would not only give you the proportion of infected women that are being identified, but also would provide the denominator for assessing the proportion of women using the prevention programs.

Monitoring ZDV use

- number of HIV+ women starting ZDV
- amount of ZDV used in program

Monitoring the use of ZDV or other antiretrovirals is not too complicated. I think at a minimum you would want to know how many women are being initiated on the regimen. You also may want to collect data on how much actual drug is being used, since that would be an important cost item.

Combining these two pieces of data might allow a low-tech approach to estimate compliance, that is, how much AZT is being used on average by women in the program. This information might provide an indication of whether more or less AZT is being used than would be expected.

There obviously are other things you might want to monitor that would require more complex data collection, such as more direct measures of adherence to the program.

Monitoring formula use

- number of HIV+ women using formula
- amount of formula used in program

There are similar issues with monitoring formula use. In addition to the number of people using the program and the amount of formula being used, some assessment of duration of use would be relevant. There may be additional important issues such as measuring the possible "spillover" of formula-feeding into the general population that would require more complicated data collection.

Evaluating program outcomes is more complicated than evaluating program coverage. The first task is to determine what outcome is relevant to monitor.

Possible infant outcomes to monitor

- number of known HIV-exposed infants born
- number of children diagnosed with HIV infection
- number of children with AIDS (esp <1 yo)
- hospitalizations, deaths

The number of known HIV-exposed infants might serve as an appropriate denominator for some possible outcome indicators. The most direct outcome measure would be HIV infection. Using HIV infection as a numerator would allow you to get some crude population-based estimates of transmission risks and how these risks are being affected by your program.

The problem with using HIV infection as an outcome is that it is difficult to measure. As most of you probably know, you cannot do a simple test at delivery to determine if the baby is infected or not; it requires some period of follow-up. There would be two approaches to this measurement. The first is to have a more substantial period of follow-up that would allow an antibody test at 1 year or more of age to determine the infection outcome. With this approach you have to consider the loss to follow-up that would occur over that year period. The second approach is to use more expensive and complicated testing that might diagnose infection earlier, but would require more resources and more sophisticated laboratories. Both approaches would require a systematic approach to diagnosing HIV infection to be useful.

Child outcome case surveillance

- considerations
  - one-time vs. longitudinal
  - complete vs. sampling
- example data items for case surveillance
  - name/ID, date and place of birth, date of diagnosis, AZT used?, age of weaning

A second possible outcome marker would be counting the number of children diagnosed with AIDS. This might be a somewhat simpler approach by using clinical diagnoses that do not require systematic testing, but it has problems. First, it is a less direct measurement, in that other factors affect the progression to AIDS so this would not be measuring transmission directly. This problem can be decreased some by limiting the outcome measure to AIDS cases that occur in children less than 1 year of age. Because children rapidly progress to AIDS, a fair proportion of children who are infected develop AIDS in the first year of life and this can be a more timely measurement.

Finally, an important issue is whether just measuring HIV infection is enough. Considering issues regarding the risks of replacement feeding in terms of the morbidity and mortality that may be induced by not breast-feeding, we need to look beyond HIV infection to other outcomes such as overall infant mortality or hospitalizations that would allow a broader measure of infant outcome.

An important approach to measuring these outcomes that should be considered is a case surveillance system that would allow you to link together pieces of program information with the outcome. Having a registry of infected children, for instance, would allow collection of certain pieces of data that would enable you to more directly assess your program coverage. That is, you could look at the infected and uninfected children and look

at what proportion of them received short-course AZT, for instance, or what proportion were breast-fed, for instance, and get a more direct assessment of efficacy.

A major consideration for case surveillance is that it is an expensive undertaking; it requires substantial commitment and resources. In addition, you need to think about other issues, such as whether it is a one-time registry of a single event, such as an HIV infection that is diagnosed, or is it a longitudinal system where you are counting HIV infection and death. Finally, whether this should be a national program or some sampling or some sentinel population that is looked at is another consideration.

Some examples of what one might collect in a sample registry that could be done on a 3-by-5 card include an identifier for where the baby was born (so you could look at the program components associated with that birth site), when the diagnosis was made, and whether or not pieces of the program, such as AZT or formula-feeding, were used. Those are the kinds of things that one could collect in a very rudimentary manner.

Other possible outcomes to measure

- adverse events possibly related to program (eg, birth defects, formula use among non-HIV population)

There are other outcomes that one may want to measure. We have mentioned a lot of potential adverse outcomes to perinatal prevention programs that at least should be considered for monitoring, such as whether or not there is any risk to taking antiretroviral medications, such as birth defects or tumors; the issue of spillover of formula-feeding to women without HIV infection; and the issue of stigmatization.

One also might want to monitor the HIV care received by women and children as another positive outcome that might come from the program, as well as other primary prevention outcomes in the uninfected pregnant population that could be monitored.

Possible data sources

- ANC or labor log books
- administrative records (eg, pharmacy)
- case registries/surveillance
- serosurveillance
- vital statistics

Moving on to thoughts about what possible data sources should be considered for such evaluations, I believe an area where existing data could be used (perhaps modified somewhat to be more useful) is log books kept for other purposes in the antenatal clinics or on the labor floors.

Second, data that may be collected for administrative purposes, such as pharmacy records or laboratory records, could also be useful.

Third, one might think of setting up new data sources, such as case registries.

Fourth, I think the same serosurveillance that we have talked about before in antenatal settings also can be useful. One also could conceive of setting up serosurveillance in populations of children that might help assess outcomes. That would be a new population for serosurveillance.

Vital statistics data can enumerate deaths and possibly collect causes of deaths that might help you understand the death outcome. Special studies, such as behavioral or epidemiologic studies, could also be considered to analyze particular problems.

Data issues

- data management, computerization
- confidentiality of data
- useful reports for feedback
- comparability of data from different sources

Finally, I would like to mention some issues related to data collection that need to be thought about. First of all, the flow of the data needs to be considered. Whenever you are talking about collecting new data you need to be thinking about where the forms are going to go. Who is going to handle them? Are you going to use computers? If so, how is that going to work? It is important to collect data in such a way that confidentiality is maintained.

You need to be summarizing data in ways that can provide routine feedback to people who will be making decisions based on these data and working with those decision-makers on formulating the best way that these reports can be formatted.

You need to consider the comparability of this somewhat uncontrolled mass of data that you might be getting from disparate sources, and what are the potential fallacies you might have in interpreting pieces of data that were not necessarily designed to work together.

Summary

- Program monitoring useful for maximizing effectiveness
- Potential for using existing data sources with some modification
- Case surveillance may be useful component

Despite all these challenges, I think that we definitely need to be thinking about these program monitoring issues at the time these programs are initiated, because they will be very important, particularly early on, in providing feedback for programs so that they can be maximally effective. We need to focus now on identifying the most useful existing data sources that could be modified to serve the purpose, but consider that there may need to be new data systems set up for such monitoring, such as case surveillance, that would require more effort.

International Plans for, and Status of, Perinatal Prevention Programs

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After the release of the results from the CDC Thai trial in early March, a meeting hosted by UNAIDS in Geneva and co-organized with WHO and UNICEF called for concerted international action to prevent the transmission of HIV from mother to child.

This meeting was attended by representatives of:

- Reproductive health and AIDS control programs where the trials and the prevention of mother-to-child transmission are ongoing. Indeed, there is an ethical imperative to support the introduction of interventions proven to be effective in countries in which trials have been completed.
- Countries where there already is a program to prevent mother-to-child transmission, namely Thailand and Brazil.
- Bilateral organizations.
- Research agencies.
- UNAIDS co-sponsors, i.e., U.N. agencies.

The meeting was held to discuss implications of the CDC Thai trial for program implementation and resource allocation in developing countries and to agree on international mechanisms for an accelerated technical development.

A statement was issued at the end of the meeting which emphasizes several points. Interventions to prevent mother-to-child transmission of HIV, including recent breakthroughs in antiretroviral therapy, offer immediate opportunities to:

- Save children's lives
- Reduce the impact of HIV on families and communities
- Strengthen maternal and child health services
- Increase access to voluntary and confidential HIV counseling and testing

The ability to make widely available, and as soon as possible, the intervention to reduce HIV transmission from mother to child depends on political will. It was thought by the meeting participants that powerful means of effective change lie in demonstrating the success of interventions to reduce mother-to-child transmission of HIV, as well as the cost of not acting to prevent this kind of transmission.

Three factors that affect the affordability of an intervention to prevent mother-to-child transmission are the cost of the drugs, the cost of adequate alternatives to breast-feeding, and the cost of the HIV tests. WHO has already added ZDV for the prevention of mother-to-child transmission to the essential drug list, and Glaxo Wellcome has recently offered ZDV at a substantially reduced price. Further negotiations are ongoing to minimize the cost of each of these components.

Service delivery, including voluntary HIV counseling and testing, represents a further set of costs. In countries with well-functioning health systems, the additional service delivery costs of interventions to reduce mother-to-child transmission may be affordable. Other countries may require more substantial investments to strengthen their health infrastructure to allow for the incorporation of large-scale interventions. Where applicable, traditional health and community support systems also should be fully utilized. Such investments will have a broad beneficial effect on the health sector more generally and should be encouraged.

The following parameters describe the optimum context in which to implement effectively the interventions necessary to reduce transmission of HIV from mother to child.

- All women should have knowledge about HIV and should have access to the information necessary to make appropriate choices about HIV prevention and about sexual and reproductive health and infant feeding in the context of HIV.
- HIV counseling should be available for pregnant women and those contemplating pregnancy. Such counseling should address the needs of pregnant women and women living with HIV, including reproductive health issues such as family planning and safe infant feeding. Active referral and/or networking for follow-up counseling, comprehensive care, and social support should be available for the HIV-positive woman and her family.
- Pregnant women and those contemplating pregnancy should have access to voluntary HIV testing, to test results with the least possible delay (requiring that appropriate laboratory services be available to process such tests), and to counseling.

- All pregnant women should have access to antenatal, delivery, and postpartum care, and a skilled attendant at birth. For the shorter ZDV regimen to be effective, at least one antenatal visit with follow-up is needed before 36 weeks, and preferably before 34 weeks of gestation.
- To benefit from this intervention, women who access antenatal services prior to 36 weeks should have access to voluntary HIV counseling and testing. Skilled care during delivery also is needed; the shorter ZDV regimen also involves administration of ZDV during labor and delivery. There should be follow-up of children, at least until 18 months, especially for nutrition and for childhood illnesses.

The efficacy of ZDV in preventing HIV transmission to the child from an HIV-positive mother who breast-feeds is currently not known. ZDV may provide some degree of protection, also probably much less than the protection it provides to infants who are not breast-fed. Since the majority of HIV-positive women facing transmission from mother to child are women who breast-feed, it is critical to resolve this issue. It also is necessary to learn more about the effect on the morbidity and mortality of infants born to HIV-positive women of introducing alternatives to breast-feeding.

Nevertheless, the greatest reduction in mother-to-child transmission of HIV is likely to occur when an integrated prevention program is implemented which combines the provision of ZDV and a safe alternative to breast-feeding. However, if a woman chooses not to use both ZDV and safe alternatives to breast-feeding, she still should have access to the intervention of her choice and should be supported to carry out the use of this intervention safely and effectively.

Other unresolved issues involve the efficacy of even shorter regimens of ZDV than that used in the Thai study and the efficacy of interventions that do not require knowledge of serostatus, such as vitamin A supplementation and vaginal cleansing for prevention of mother-to-child transmission. Results from ongoing research will indicate whether or not these can be proposed as effective interventions on their own.

Additional research is also required on issues such as factors influencing the uptake of voluntary counseling and testing, not returning for HIV test results, adherence to the regimen, and acceptance of interventions to prevent mother-to-child transmission.

Recognizing the urgency of the situation and at the same time the fact that it will take time to mobilize new resources for these interventions, it is recommended that a phased approach be taken in the introduction of such interventions. Such an approach will tailor implementation to utilize fully and immediately existing national and local capacities, with a concrete plan to build on these initial efforts over time. Where the capacity to implement these interventions is limited, efforts should begin immediately to increase capacity, with a plan to introduce these interventions as soon as possible.

Mechanisms are being established through UNAIDS in close collaboration with UNICEF and WHO to coordinate and support efforts for accelerated capacity strengthening and technical development, and to scale up the implementation of interventions to reduce

mother-to-child transmission. These mechanisms will facilitate the exchange of information, mobilize resources, help to coordinate research, and resolve remaining policy, programmatic, and technical issues.

After the March meeting, UNAIDS, WHO, and UNICEF decided that the most important functions for an international initiative would be:

- Communication and advocacy
- Accelerated technical development, including support to resolve remaining important research questions and the development of precise recommendations regarding drug regimen to be used, test kits, counseling needs, and adequate replacement feedings
- Implementation of pilot projects in sites selected according to criteria such as HIV prevalence, capacity to support new interventions, and capacity to share the experience with neighboring countries

These projects should be carefully monitored and evaluated to refine our strategies and learn while doing. However, these projects should be viewed not just as pilot studies, but rather as starting phases before expanding the interventions.

Some of the mechanisms of coordination that are being set up include a network of institutions, governmental and nongovernmental, involved in technical development and implementation of interventions. This will allow exchange of material and identification of gaps, but also will provide opportunities to create collaboration between institutions working on a specific topic, such as HIV testing and counseling, and of institutions working in a given geographical area. Following this idea, UNICEF is organizing a regional workshop in Eastern Africa next September to create a regional dynamic.